Methods: INFUSE AMI randomized 452 patients with anterior STEMI undergoing primary PCI with bivalirudin anticoagulation to intralesion (IL) bolus abciximab vs. no abciximab and to thrombus aspiration vs. no aspiration. The primary endpoint was cMRI infarct size (IS, % of left ventricular mass) at 30 days. At the clinician's discretion 297 patients were treated with clopidogrel (Clop) and 155 patients with prasugrel (Pras). Clinical outcomes were compared using propensity adjusted analyses incorporating clinical and angiographic variables relevant to drug selection.
Results: Clop patients were significantly older (62.7y ± 12.7 vs. 57.6y ± 10.4, P<0.0001) and had lower EF (40.5% ± 10.4 vs. 47.4% ± 13.7, P<0.0001) than Pras patients. The two groups achieved similar rates of successful reperfusion: TIMI 3 flow - 89.6% vs. 94.8%, P=0.06, MBG 2 or 3 - 80.4% vs. 83.2%, P=0.46. IS was significantly smaller in Pras patients (16.4% [6.5, 20.0] vs. 17.6% [8.1, 25.7], P=0.05). The incidence of definite or probable stent thrombosis at 24 h and 1 year was 0% vs. 0.3%, P=0.47 and 0% vs. 2.5%, P=0.05, respectively. The propensity adjusted hazard ratios for clinical events to 12 months follow-up are shown in Table.

Clinical Event	Adjusted HR (95% CI) Pras vs Clop	P value
Death	0.18 [0.04, 0.86]	0.03
Death/MI	0.16 [0.03, 0.76]	0.02
Horizons-Defined Major Bleeding	2.09 [0.70, 6.21]	0.18
MACCE	0.37 [0.13, 1.03]	0.06
MACE	0.33 [0.12, 0.96]	0.04
Clinically Driven TVR	0.76 [0.18, 3.17]	0.7

Conclusions: In this propensity adjusted analysis from the largest yet reported cohort of STEMI patients undergoing bivalirudin supported primary PCI, there appears to be a benefit of treatment with prasugrel rather than clopidogrel with respect to infarct size and 1-year clinical events, including death and stent thrombosis.

TCT-4

Efficacy and Safety of Concurrent Administration of Clopidogrel-loading (600mg) and Prasugrel-loading (60mg) in Patients with Acute ST-Segment Elevation Myocardial Infarction

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Background: Current STEMI guideline recommendations limit the use of prasugrel to clopidogrel-naïve patients. However, in daily clinical practice a considerable proportion of STEMI patients undergoing primary PCI are preloaded with clopidogrel. Whether the use of prasugrel in clopidogrel pretreated STEMI patients is safe remains unknown. Similarly, the efficacy of a combined loading dose regimen has not been evaluated.
Methods: Between 1 September 2009 and 15 October 2012, a total of 1,157 STEMI patients were included in the randomized COMFORTABLE AMI trial (NCT 00962416) and 891 STEMI patients in the SPUM ACS registry (NCT 01000701) at 12 centers. Patients were divided into three groups according to type of peri-procedural antiplatelet loading: (1) Clopidogrel and subsequent Prasugrel loading dose [CP], (2) Prasugrel loading dose alone [P] (3) Clopidogrel loading dose alone [C]; 23 patients were excluded because they were not exposed to Clopidogrel and Prasugrel. The primary safety endpoint was the rate of BARC type 3, 4 and 5 bleeding at 30 days. The primary efficacy endpoint was the composite of cardiac death, nonfatal MI and nonfatal stroke at 30 days. Outcomes were analyzed using Cox's Regressions (crude) and multinomial ITPW weighted Cox's Regressions.
Results: A total of 2,025 patients were analysed of whom 428 (21.1%) had received CP, 447 (22.1%) patients P alone, and 1,150 (56.8%) patients C alone. The primary safety endpoint was observed among 1.2% of CP, 1.6% of P, and 1.5% of C patients (CP vs C ad. HR 0.99 (0.36-2.72), PC vs P ad. HR 0.73 (0.22-2.41). The primary safety endpoint occurred less frequently among CP (1.9%) compared with C patients (5.0%, adjusted HR 0.47 (0.22-1.00), but with similar frequency among P and C patients (2.9% vs 5.0%, ad. HR 0.68 (0.27-1.73). The net clinical benefit outcome parameter tended to be lower among CP (2.8%) compared with C patients (6.3%, ad. HR 0.56 (0.30-1.05), whereas no significant difference was observed between P and C patients (3.8% vs 6.3%, ad. HR 0.85 (0.39-1.86).
Conclusions: Among STEMI patients preloaded with Clopidogrel, the concurrent administration of a Prasugrel loading dose appears safe and potentially more effective than Clopiogrel alone.

TCT-5

Relationship Between High Platelet Reactivity on Clopidogrel and Outcomes After DES Implantation: Two-Year Results From the ADAPT-DES Study

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Background: In the large-scale, prospective, multicenter ADAPT-DES study, we previously demonstrated that at 1 year, high platelet reactivity (HPR) to clopidogrel (PRU >208) was strongly associated with stent thrombosis (ST) after DES, but was protective against major bleeding, and that both impacted mortality such that PRU >208 was not associated with death. DAPT was recommended for at least 1 year in this study. We herein report the ADAPT-DES results at 2-year follow-up.
Methods: VerifyNow P2Y12 assay was performed after successful DES implantation in 8,448 "all-comers" patients enrolled at 11 US and European sites. Univariable and propensity-adjusted multivariable analyses were performed to determine the relationship between HPR and subsequent events.
Results: Median age was 64 years, 25.6% were female, 32.3% had diabetes, and 51.4% (9.6% STEMI) presented with an acute coronary syndrome. HPR on clopidogrel, defined as PRU >208, was present in 42.7% of patients. Aspirin use at 1 year, 2 years, and daily without discontinuation through 2 years were 95.3%, 93.4%, and 82.2%, respectively. Corresponding values for thienopyridine use were 83.8%, 56.8%, and 49.0%. At 2 years, target lesion ST occurred in 77 (0.94%) patients, MI occurred in 383 patients (4.73%), major bleeding in 721 patients (8.53%), and death in 306 patients (3.81%). In a fully adjusted multivariable model including propensity score stratification for PRU, HPR at 2 years was independently associated with ST (rate 1.4% vs 0.6%, adjusted HR 2.01, p=0.007) and MI (5.7% vs 4.0%, adjusted HR 1.32, p=0.01), was protective against major bleeding (8.1% vs. 8.8%, adjusted HR 0.79, p=0.004), and was not associated with death (4.8% vs 3.1%, adjusted HR 1.22, p=0.11). HPR was not associated with ST, MI, or death between years 1 and 2. Of 12 patients with very late target lesion ST, 10/12 (83%) were on DAPT at the time of the event.
Conclusions: In the present large-scale study, HPR on clopidogrel after DES implantation was an independent predictor of 2-year ST and MI, and was inversely correlated with major bleeding. HPR was not independently correlated to adverse events between years 1 and 2 or all-cause 2-year mortality.